Respiratory Medicine (2007) **101**, 2091–2098

ELSEVIER

respiratoryMEDICINE

Epidemiology of acute lung injury and acute respiratory distress syndrome in The Netherlands: A survey

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Received 14 March 2007; accepted 25 May 2007
Available online 9 July 2007

KEYWORDS
Defining ALI/ARDS;
ICU planning;
ALI/ARDS incidence;
Risk factors;
Aspiration pneumonia;
Geographical differences

Summary
Background: The characteristics, incidence and risk factors for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) may depend on definitions and geography.
Methods: A prospective, 3-day point-prevalence study was performed by a survey of all intensive care units (ICU) in the Netherlands ($n = 96$). Thirty-six ICU's responded (37%), reporting on 266 patients, of whom 151 were mechanically ventilated. The questionnaire included criteria and potential risk factors for ALI/ARDS, according to the North American–European Consensus Conference (NAECC) or the lung injury score (LIS $\geqslant$ 2.5).
Results: Agreement between definitions was fair (κ 0.31–0.42, $P = 0.001$). ALI/ARDS was characterized, regardless of definition, by radiographic densities, low oxygenation ratios, high inspiratory O_2 and airway pressure requirements. Depending on definitions, ALI and ARDS accounted for about 12–33% and 7–9% of ICU admissions per year, respectively, constituting 21–58% (ALI) and 13–16% (ARDS) of all mechanically ventilated patients. The annual incidences of ALI and ARDS are 29.3 (95%CI 18.4–40.1) and 24.0 (95%CI 14.2–33.8) by NAECC, respectively, and are, respectively, 83.6 (95%CI 65.3–101.9) and 20.9 (95%CI

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0954-6111/$ - see front matter
doi:10.1016/j.rmed.2007.05.021

11.7–30.1) by LIS per 100,000. Risk factors for ALI/ARDS were aspiration, pneumonia, sepsis and chronic alcohol abuse (the latter only by NAECC).
Conclusion: The effect of definitions of ALI/ARDS on mechanical ventilation in the Netherlands is small. Nevertheless, the incidence of ALI/ARDS may be higher than in other European countries but lower than in the USA, and the incidence of ALI by LIS may overestimate compared to that by NAECC. Aspiration, pneumonia, sepsis and chronic alcohol abuse are major risk factors, largely independent of definitions.

Introduction

Acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) are common causes of respiratory insufficiency and need for mechanical ventilation in the intensive care unit (ICU). The syndromes are associated with a high mortality rate, varying between 30% and 60%, while ARDS may be the tip of the iceberg of ALI.[1–26]

The syndromes can be clinically defined either according to the criteria from the North American European Consensus Conference (NAECC) or according to the lung injury score (LIS).[4–10,12–15,18,20–23,26–32] Although the NAECC criteria can be regarded as the reference standard, LIS-based definitions are less dependent on haemodynamic criteria, which are often neglected since they may be hard to obtain. The LIS depends more on ventilatory variables, including positive end-expiratory pressure (PEEP) ventilation. Absence of PEEP in the NAECC definition renders the oxygenation ratio of arterial PO_2 (P_aO_2) to inspiratory O_2 fraction (F_IO_2) a poor criterion, since the ratio is affected by PEEP.[16,33,34] Nevertheless, agreement of these diagnostic systems may be fair, in terms of epidemiology, diagnostics, and outcome.[7,12,18,29] Finally, the characteristics of ALI/ARDS patients conforming to the above definitions (as compared to patients without the syndromes) are only rarely described.[14,16,22,25,33,34]

The reported incidence of ALI/ARDS ranges from 1.5 to 100 per 100,000 person-years, depending on study methodology, definitions and geography, among others.[1,2,5,10–14,20,21,23,25,26,28,30,35] There are no data available for the Netherlands, unlike for other European countries,[2,3,5,12,14,15,25] that could help health care planning and trial design. The definitions of ALI/ARDS include the presence of recognized risk factors. Direct risk factors include sepsis, trauma, multiple transfusions, aspiration, pulmonary contusion, pneumonia and near drowning, among others, and indirect risk factors include old age and chronic alcohol abuse, while a history of diabetes mellitus may protect.[1,3,4,6,7,10,12–16,20–22,24–26,29–31,36,37] The risk factors for ALI/ARDS may also depend on definitions.[29,30] For instance, chronic alcohol abuse was a risk factor when using the NAECC criteria to diagnose ARDS, but perhaps less clearly when other definitions were used.[17,19,38]

The aims of the current study were to determine the characteristics and incidence of ALI/ARDS on the ICU's in the Netherlands, to identify direct and indirect risk factors for the syndrome, to evaluate dependence on definitions, and to compare data with the literature.

Patients and methods

This is a prospective postal survey of all Dutch ICUs ($n = 96$, spread over about 100 hospitals) with a total of 827 beds. The number of intensive care beds has not changed in the Netherlands since 2000, while the Dutch population was estimated as 15,987,075 at the time of the study. In October of that year, after publication of the ARDS network landmark study on low tidal volumes,[39] treating physicians on these ICUs were requested to fill out a questionnaire concerning the respiratory status of their ICU patients, at noon on each of 3 consecutive days. Analyses were updated in 2005 in view of recent literature on epidemiology and diagnostics of ALI/ARDS.[26,40] Two institutional ethical review boards approved of the study design. We only report on the patients who were intubated and mechanically ventilated. Variables recorded were demographic data, such as age and sex, comorbidity, recent surgery (within 2 weeks prior to admission) and reasons of admission. Other data included the length of stay in the hospital prior to inclusion, the Acute Physiology and Chronic Health Evaluation II (APACHE II)[37] score, the causes of respiratory insufficiency necessitating mechanical ventilation and the presence of possible risk factors for ALI/ARDS, judged by the treating physician according to international classification codes of disease (ICD-10). The mean of values, recorded within 2 h before daily assessment of patients, for haemodynamic, gasometric variables and ventilatory settings were evaluated. We also included chest radiographic and echocardiographic data and treatment with diuretics, inotropes/vasopressors and corticosteroids, as well as culture results, within 2 days prior to the first study day. To determine the presence of ALI/ARDS, the NAECC and LIS criteria were used to classify patients by two independent investigators (J.W., J.V.), on the first day and a complete data set is available for evaluation. The NAECC criteria for ARDS include the presence of a known risk factor, a $P_aO_2/F_IO_2 \leqslant 200$ mmHg regardless of the level of positive end-expiratory pressure (PEEP), recent-onset bilateral pulmonary infiltrates compatible with pulmonary oedema, in the absence of evidence for a hydrostatic cause (pulmonary capillary wedge-pressure $\leqslant 18$ mmHg or the absence of clinical evidence of left heart failure), and absence of other causes of the respiratory insufficiency such as atelectasis and pleural fluid.[27] In many cases, a pulmonary artery catheter was not used and the pulmonary capillary wedge pressure (PCWP) was, therefore, unavailable, as reported before.[40] Instead, a central venous

pressure <15 cm H_2O or the results of echocardiography (including dysfunction of the left ventricle such as dilatation or wall motion abnormalities), if available, were used to decide on ARDS according to the NAECC criteria, in accordance with recent literature.[40] To decide on ARDS according to the LIS criteria (ranging between 0 and 4), a recognized risk factor should be present, together with a LIS score $\geqslant 2.5$.[7,12,29–32] The LIS is determined by four criteria, each graded on a four-point scale, including the number of quadrants with alveolar densities on chest radiography, the P_aO_2/F_IO_2 ratio, the level of PEEP and the total respiratory dynamic compliance. The latter was calculated from ventilatory settings. ALI was defined according to the NAECC criteria except for a P_aO_2/F_IO_2 ratio <300 mm Hg[27] and according to the LIS score >1.[32]

Calculations and statistical analysis

The prevalence of ALI/ARDS on the responding ICUs, the total number of ICU beds and population in the Netherlands, and the average ICU length of stay for patients with ALI/ARDS, i.e. 16.7 days, were used to estimate the annual incidence. The mean length of stay was calculated using that of survivors and non-survivors and the mortality ratio in recent American and European ALI/ARDS studies and one study by our group, using the[67] Gallium scan as a reference standard for defining ALI/ARDS.[9,14,24] The level of chance-corrected agreement between ALI/ARDS defined by NAECC and LIS criteria was expressed as κ. Continuous data were compared with a Student's t-test, while the Fisher's exact and χ^2-tests were used to compare frequencies. Risks are expressed as odds ratios (OR) with 95% confidence intervals (CI). To find the smallest set of independent predictors of ARDS defined by NAECC or LIS, multiple logistic regression was done on the basis of the likelihood ratio using a backward procedure after entering risk factors, with $P<0.10$ in univariate analyses. This yielded adjusted ORs and 95%CIs. Goodness of fit was evaluated by the Hosmer–Lemeshow test. Continuous data are summarized by mean (standard deviation, SD). A two-sided $P<0.05$ was considered as statistically significant. Exact P-values are given unless <0.001.

Results

Hospitals and ICUs

Of the 96 adult ICUs mailed, 36 responded (37%) from 32 regional and 4 academic hospitals, reporting on 266 patients (in 33% of the ICU beds), of whom 151 were mechanically ventilated during the study (Tables 1 and 2 and 2A, additional material).

Table 1 Responding and non-responding intensive care units (ICUs).

	Responding ($n=36$)	Non-responding ICU ($n=60$)
Number of beds per hospital	504 (180–1000)	387 (102–1221)
Total number of ICU beds	9 (4–60)	8 (1–40)
ICU level (% of ICUs)		
1	23%	40%
2	63%	50%
3	13%	10%
University hospital	3 (8%)	5 (8%)

Mean (range) or number and percentage where appropriate. ICU level: level 3 large, highly staffed and equipped ICU, level 1 small, lowly staffed and equipped ICU, according to national guidelines. There were no differences.

Definitions and agreement

Of the 151 patients, 31 met the NAECC and 88 the LIS criteria for ALI, i.e. 12–33% of ICU-admitted patients and 21–58% of mechanically ventilated patients. Thirty-one patients met both definitions and 63 patients did not ($\kappa = 0.31$, $P<0.001$). Fifty-seven were classified as having ALI according to the LIS and but not by the NAECC, while the opposite did not occur. In the 31 patients with ALI according to the NAECC, hydrostatic or cardiogenic oedema was unlikely on the basis of a low PCWP ($n=1$), a low CVP ($n=24$), echocardiographic findings ($n=2$) or clinical information ($n=4$). In 10 LIS-defined ALI patients, 3 of 4 LIS criteria only were available. Of the 151 patients, 24 met the NAECC and 20 the LIS criteria for ARDS, i.e. 7–9% of ICU-admitted and 13–16% of mechanically ventilated ICU patients. Eleven patients met both definitions and 118 patients did not. Nine patients were classified as having ARDS according to the LIS but not the NAECC, while the opposite occurred in 13 patients ($\kappa = 0.42$, $P=0.001$). In the 24 patients with ARDS according to the NAECC, hydrostatic or cardiogenic oedema was unlikely on the basis of a low PCWP ($n=1$), a low CVP ($n=19$), echocardiography ($n=1$) or clinical information ($n=3$). In one LIS-defined ARDS patient, three of four LIS criteria only were available (Table 3).

Patient and respiratory characteristics

In Tables 2 and 2A, additional material, demographic and clinical data are presented for ALI/non-ALI and ARDS/non-ARDS patients, respectively, according to the NAECC and LIS definitions. When the results for chest radiography are compared (Tables 3 and 3A, additional material), patients with ALI/ARDS according to the NAECC or LIS definitions had more (often) alveolar consolidations or interstitial abnormalities than those without. Pulmonary oedema was particularly manifest in ARDS (LIS criteria). In the patients with ALI/ARDS according to the NAECC or the LIS criteria, the PEEP was higher and the oxygenation ratio lower than in patients without ALI/ARDS. Total respiratory dynamic compliance was particularly low in patients with ALI/ARDS according to LIS. Tidal volumes averaged 8.4 mL/kg.

Table 2 Demographic and clinical data for acute lung injury.

	NAECC			LIS		
	ALI ($n = 31$)	No ALI ($n = 120$)	P	ALI ($n = 88$)	No ALI ($n = 63$)	P
Demographics						
Age (years)	58 (18)	62 (15)	0.39	62 (15)	60 (17)	0.67
Gender, m/f	23 (74)/8 (26)	77 (64)/43 (36)	0.40	55 (63)/33 (38)	45 (71)/18 (29)	0.30
APACHE II	22 (6)	18 (9)	0.16	21 (8)	15 (7)	0.01
Days before inclusion	8 (7)	10 (13)	0.86	9 (11)	11 (13)	0.66
Reasons for ICU admission						
Respiratory insufficiency	15 (48)	37 (31)	0.09	37 (42)	15 (24)	0.04
After surgery	4 (13)	38 (32)	0.04	20 (23)	22 (35)	0.10
Sepsis	6 (19)	12 (10)	0.21	13 (15)	5 (8)	0.31
Trauma	2 (6)	12 (10)	0.74	8 (10)	6 (10)	1.00
Shock	0	5 (4)	0.58	4 (5)	1 (2)	0.65
Cardiac	2 (6)	12 (10)	0.74	7 (8)	7 (11)	0.57
Neurological	1 (3)	9 (8)	0.69	5 (6)	5 (8)	0.74
Miscellaneous	4 (13)	8 (7)	0.27	7 (8)	5 (8)	1.00
Haemodynamic, metabolic and therapeutic variables						
Systolic BP (mmHg)	127 (21)	130 (25)	0.34	125 (23)	135 (26)	0.02
Diastolic BP (mmHg)	63 (13)	64 (12)	0.42	62 (12)	66 (13)	0.05
CVP (mmHg)	9 (4) ($n = 24$)	10 (5) ($n = 71$)	0.41	10 (5) ($n = 60$)	9 (6) ($n = 35$)	0.22
PCWP (mmHg)	12 ($n = 1$)	15 (6) ($n = 14$)	0.56	14 (3) ($n = 9$)	16 (10) ($n = 6$)	0.91
pH	7.4 (0.1)	7.4 (0.1)	0.56	7.4 (0.1)	7.4 (0.1)	0.44
Bicarbonate (mmol/L)	26 (7)	25 (5)	0.22	26 (6)	24 (5)	0.38
Inotropes/vasopressors	14 (45)	50 (42)	0.84	47 (53)	17 (27)	<0.001
Corticosteroids	14 (45)	30 (25)	0.05	32 (36)	12 (20)	0.04
Diuretics	10 (32)	39 (33)	1.00	31 (35)	18 (29)	0.48
Infection						
Positive cultures	12 (38)	19 (16)	0.01	27 (31)	4 (6)	<0.001

Mean (SD) or number (percentage), where appropriate; abbreviations: NAECC, North American–European consensus conference; LIS, lung injury score; ALI, acute lung injury; APACHE, acute physiology and chronic health evaluation II; ICU, intensive care unit; BP, blood pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure.

Incidence

The annual incidences (per 100,000) of ALI and ARDS in the Netherlands are, respectively, 29.3 (95%CI 18.4–40.1) and 24.0 (95%CI 14.2–33.8) according to NAECC criteria and are, respectively, 83.6 (95%CI 65.3–101.9) and 20.9 (95%CI 11.7–30.1) according to LIS criteria. Hence, ALI and ARDS account, respectively, for 4684 (95%CI 2941–6422) and 3837 (95%CI 2270–5403) annual ICU admissions according to the NAECC criteria and, respectively, for 13,365 (95%CI 10,440–16,291) and 3341 (95%CI 1871–4812) ICU admissions according to the LIS criteria.

Risk factors (Tables 4, 4A and 5, 5A, additional material)

Aspiration, pneumonia and sepsis were major direct risk factors for ALI/ARDS, relatively independent of definitions used. In contrast, chronic alcohol abuse was an independent risk factor for ARDS only when defined by NAECC. The risk to develop ALI (NAECC) increased ($P = 0.008$) with the number of risk factors from 5% without to 100% with four or five risk factors; the risk for ALI (LIS) increased ($P = 0.003$) from 34% without risk factors to 100% with four or five factors. Also, the risk to develop ARDS defined by NAECC or LIS increased with the number of risk factors (Fig. 1A and B).

Discussion

In this study, we tried to characterize and estimate the incidence of ALI/ARDS necessitating mechanical ventilation in the ICU in the Netherlands. Aspiration, pneumonia, sepsis and chronic alcohol abuse are major risk factors for the syndromes. The data suggest small effect of definitions only.

The moderate agreement between definitions of ALI/ARDS according to the NAECC and LIS criteria, which otherwise agrees with the literature,[12,18,29] can be explained since the LIS is a severity score, while the NAECC criteria are designed for diagnostic purposes only.[5,7,8,24,27,29,32] Moreover, clinically manifest hydrostatic and cardiogenic causes of pulmonary oedema are excluded by the NAECC and not necessarily by the LIS, by virtue of the criteria. Otherwise, the low use of pulmonary artery catheters and varying information used to rule out hydrostatic or cardiogenic

Table 3 Respiratory characteristics for acute lung injury.

	NAECC			LIS		
	ALI ($n = 31$)	No ALI ($n = 120$)	P	ALI ($n = 88$)	No ALI ($n = 63$)	P
Chest X-ray						
Normal	0	21 (18)	0.01	3 (3)	18 (29)	<0.001
Alveolar/interstitial abnormalities	28 (90)	31 (26)	<0.001	54 (61)	5 (8)	<0.001
Number of quadrants	3 (2–4)	2 (0–4)	<0.001	3 (1–4)	2 (0–4)	0.14
Oedema	3 (10)	2 (2)	0.07	5 (6)	0	0.08
Pleural effusion	5 (16)	36 (30)	0.12	21 (24)	20 (32)	0.20
Atelectasis	2 (7)	27 (23)	0.04	17 (19)	12 (20)	1.00
COPD	1 (3)	8 (7)	0.68	3 (3)	6 (10)	0.16
Lung function						
F_IO_2	0.51 (0.11)	0.43 (0.12)	<0.001	0.49 (0.13)	0.39 (0.08)	<0.001
P_aO_2/F_IO_2 (mmHg)	173 (50)	239 (86)	<0.001	184 (58)	283 (81)	<0.001
P_{plat} (cm H_2O)	26 (10)	18 (8)	0.01	24 (9)	15 (6)	<0.001
PEEP (cm H_2O)	8 (3)	7 (3)	0.01	8 (4)	5 (2)	<0.001
Tidal volume (mL)	577 (133)	597 (154)	0.71	573 (123)	621 (180)	0.18
$Compliance_{tot\ respir}$ (mL/cm H_2O)	41 (25)	60 (59)	0.18	37 (19)	84 (74)	<0.001
Lung injury score	2.3 (0.5)	1.2 (0.7)	<0.001	2.0 (0.6)	0.7 (0.3)	na

Number (percentage) or mean (standard deviation), where appropriate; NAECC, North American–European consensus conference; LIS, lung injury score; ALI, acute lung injury; COPD, chronic obstructive lung disease; F_IO_2, inspiratory O_2 fraction; P_aO_2, arterial partial O_2 pressure; P_{plat}, inspiratory plateau pressure; PEEP, positive end-expiratory pressure; $Compliance_{tot\ respir}$, total respiratory compliance; na, not applicable.

Table 4 Risk factors for acute lung injury: univariate analysis.

Risk factor	NAECC			LIS			Odds ratio (95% CI)	
	ALI ($n = 31$)	No ALI ($n = 120$)	P	ALI ($n = 88$)	No ALI ($n = 63$)	P	NAECC	LIS
Direct								
Aspiration	7 (22)	6 (5)	0.01	11 (130)	2 (3)	0.07	5.5 (1.7–18.0)	4.3 (0.9–20.4)
Pneumonia	16 (52)	38 (32)	0.06	44 (50)	10 (16)	<0.001	2.3 (1.0–5.1)	5.3 (2.4–11.7)
Sepsis	16 (52)	28 (23)	0.004	34 (39)	10 (16)	0.003	3.5 (1.5–8.0)	3.3 (1.5–7.4)
Pancreatitis	1 (3)	2 (2)	0.50	2 (2)	1 (2)	1.00	2.0 (0.2–22.4)	1.4 (0.1–16.2)
Multiple trauma	3 (10)	18 (15)	0.57	12 (14)	9 (14)	1.00	0.6 (0.2–2.2)	0.9 (0.4–2.4)
Multiple blood transfusions	1 (3)	3 (2.5)	1.0	3 (3)	1 (2)	0.64	1.3 (0.1–12.9)	2.2 (0.2–21.6)
Post surgery	9 (29)	50 (42)	0.22	30 (34)	29 (46)	0.18	0.6 (0.2–1.3)	0.6 (0.3–1.2)
Post cardiac surgery	1 (3)	13 (11)	0.30	6 (7)	8 (13)	0.26	0.3 (0.03–2.2)	0.5 (0.2–1.5)
Shock	0	13 (11)	0.07	5 (6)	8 (13)	0.15	–	0.4 (0.1–1.3)
Indirect								
Chronic alcohol abuse	3 (10)	2 (2)	0.06	1 (1)	4 (6)	0.40	6.3 (1.0–39.6)	3.0 (0.3–27.1)
Diabetes mellitus	2 (6)	5 (4.2)	0.63	3 (3)	4 (6)	0.45	1.6 (0.3–8.6)	0.5 (0.1–2.4)

Number (percentage): patients can have more than one risk factor for developing acute lung injury (ALI); NAECC, North American–European consensus conference; LIS, lung injury score; CI, confidence interval.

causes of pulmonary oedema, is in agreement with the literature.[2,26,29,35,40] The P_aO_2/F_IO_2 ratio as an ALI/ARDS (NAECC and LIS) criterion is affected by PEEP, which is only included in the LIS as a criterion. The PEEP affects the ratio, and ventilatory settings thus affect meeting NAECC, but not LIS, criteria.[16,33,34] Conversely, this factor was a major reason to include the LIS in this study on mechanically ventilated patients.[16,33,34] Nevertheless, the fact that the

diagnostic systems only partially overlapped did not have a major effect on patient characteristics, incidences and risk factors for ALI/ARDS, in agreement with the some literature,[7,12,18,20,29] even though the LIS (>1)-based ALI incidence may have overestimated that of NAECC-defined ALI. Alternatively, a risk for ALI (LIS) of 34% in the absence of commonly recognized risk factors may imply yet unidentified factors.[6] Obviously, the latter phenomena would have been circumvented if a higher LIS cutoff value had been used. Otherwise, ALI/ARDS was characterized in our study, conform with the literature,[4,7,12,14,16,20,22,29,33–35] by radiographic densities, low oxygenation ratios and compliances, and high inspiratory O_2 and airway pressure requirements, while admission demographics may not differ between ALI/ARDS and non-ALI/ARDS patients, except for hypotension and vasopressor requirements that may be more common in LIS-defined ALI patients. The latter agrees with literature indicating shock as a risk factor.[4,22,25] Moreover, ALI and ARDS characteristics may not differ much, even though the latter may be more strictly defined than the former and the associated severity and mortality may be higher.[7,8,12,15,16,25,33,34,37] The use of corticosteroids associated with LIS-based ALI may have been caused by low-dose steroid treatment for vasopressor-dependent septic shock.

Table 5 Risk factors for acute lung injury: multivariate analysis.

Risk factor	Adjusted odds ratio (95% CI)	
	NAECC	LIS
Aspiration	3.5 (1.0–12.3)	
Pneumonia		6.0 (2.6–13.8)
Sepsis	4.0 (1.6–9.7)	4.2 (1.7–10.2)

NAECC, North American–European consensus conference; LIS, lung injury score; CI, confidence interval; multiple logistic regression: Hosmer–Lemeshow $P = 0.56$ for NAECC and $P = 0.84$ for LIS.

Our estimates for the annual incidence of ALI/ARDS in the Netherlands should be compared to those elsewhere.[2,3,10–14,20–23,25,26,28,30] The incidence of ALI/ARDS ranges from 1.5 to 13.5 per 100,000 in Europe[2,3,5,12,14,25] and from 1.5 to 100 in Australia and USA,[10,11,13,20,21,23,26,28,30,35] depending on study design, methodology, definitions and populations. Obviously, the incidence of ALI is somewhat higher than of ARDS.[12,15,20,23,26,31] Indeed, the ALI (NAECC criteria) incidence was recently estimated at about 80 per 100,000 person-year in the USA,[26] while our estimate on the basis of NAECC criteria agrees with earlier estimates of 22–34 per 100,000 person-year.[20,23] A comparison with the literature is hard, however. Many studies lack external validation of physician-delivered diagnoses or ICD-9 codes,[11,19,21,25] while physicians may not strictly adhere to accepted criteria and tend to overestimate occurrence of ALI/ARDS at the bedside, when defined by objective criteria.[17,28,35,41] Indeed, our study carries the advantage of post hoc evaluations of ALI/ARDS, according to two sets of criteria, as done before in some studies only.[7,10,12,17,18,28] Finally, our study was prospective, while some others were retrospective.[2,14,17,21] Some studies used even more strict NAECC criteria than we did.[3,28,29] While avoiding overestimation, these factors may have contributed to somewhat higher ALI/ARDS incidences than in other parts of Europe, but lower than those in the USA.

In accordance with the literature,[1,3,4,6–8,10,12–16,18,20–22,24–26,29–31,36,37,42] pneumonia/sepsis and aspiration were the most common aetiologic factors for ALI/ARDS. Pneumonia/sepsis (and positive cultures) and aspiration carried the greatest risk for ALI and ARDS, respectively, as suggested before.[1,21] The risk factors for ALI and ARDS may be similar and relatively independent of definitions, in support of prior

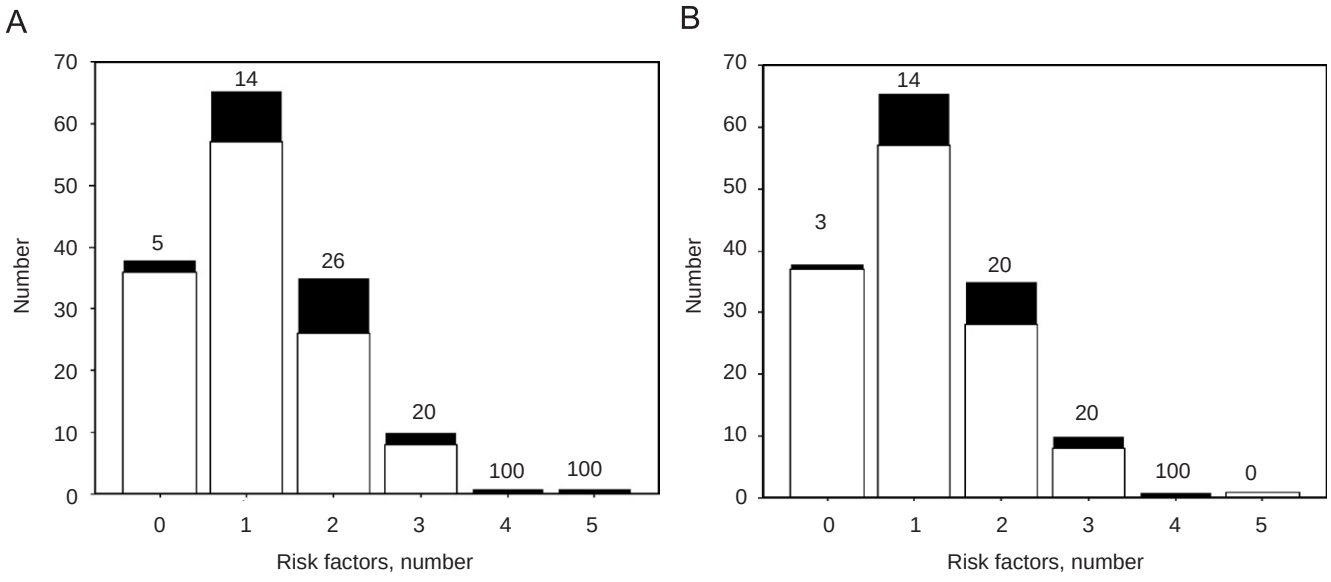

Figure 1 Number of risk factors on *x*-axis and associated frequency of ARDS in the study cohort with percentage above bars when ARDS was defined on the basis of (A) the North American–European consensus conference criteria ($P = 0.005$) and (B) lung injury score criteria ($P = 0.032$). Filled bars: ARDS; open bars: non-ARDS.

work[12,18,20,34] but in contrast to other suggestions.[16,30] The increasing risk for ALI/ARDS with a greater number of risk factors, regardless of definitions, is in agreement with the literature,[6,25,36] and supports causative roles. In our study, chronic alcohol abuse was a risk factor for ARDS according to the NAECC criteria only. The ARDS definition dependence of chronic alcohol abuse as a risk factor may thus partly explain the controversy in the literature.[17,19,38] Diabetes mellitus was not a risk factor for ARDS in our study, in contrast to its protective role in other studies.[42] This can be explained by diabetes mellitus causing impaired neutrophil function or altered neutrophil–endothelial interactions and by tight control of glycemia and thus preserved neutrophil function in patients residing in our country. Finally, advanced age did not seem to increase the risk for ARDS as in other reports,[1,36] in contrast to some studies.[6,13,17]

A limitation of our study is that, by virtue of study design, the temporal relation between onset of a risk factor and ARDS could not be determined. We cannot exclude that relatively high tidal volumes in some patients may have been harmful and contributed to the syndrome.[39] However, the mean tidal volumes used are not excessively high and conform to the literature.[21,25,33,34,39] The incidence estimation depended on some assumptions. Only inclusion of mechanically ventilated patients has commonly been done before,[5,7,12,15,18,25,26,29,31] so that comparison with the literature is allowed. We were not able to correct for migration and cannot judge seasonal influences in our incidence estimations.[12,21] Nevertheless, the response can be considered as representative for Dutch ICUs (Table 1).

In conclusion, our data on the characteristics, incidence and risk factors for ALI/ARDS necessitating mechanical ventilation in the ICU, suggest minor dependence on ARDS definitions. The data may help health care planning and trial design.

Conflict of interest

All authors do not have any financial and personal relationships with people or organizations that could inappropriately influence their work.

Acknowledgements

We like to thank all physicians working on ICU's in the Netherlands and participating in this study.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.rmed.2007.05.021.

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